



## Selección de Resúmenes de Menopausia

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### **Cognitive effects of estradiol after menopause: A randomized trial of the timing hypothesis.**

Henderson VW, St John JA, Hodis H, McCleary CA, Stanczyk F, Shoupe D, Kono N, Dustin L, Allayee H, Mack WJ.

**OBJECTIVE:** To test the hypothesis that effects of estrogen-containing hormone therapy on cognitive abilities differ between postmenopausal women near to, and further from, menopause. **METHODS:** In this randomized, double-blind, placebo-controlled trial, healthy women within 6 years of menopause or 10+ years after menopause were randomly assigned to oral 17 $\beta$ -estradiol 1 mg/d or placebo. Women with a uterus received cyclic micronized progesterone vaginal gel or placebo. The primary outcome assessed at 2.5 and 5 years, compared between treatment groups, was change in a standardized composite of neuropsychological test scores assessing verbal episodic memory. Secondary outcomes assessed executive functions and global cognition. **RESULTS:** A total of 567 women were included in modified intention-to-treat analyses after a mean treatment duration of 57 months. For verbal memory, the mean estradiol minus placebo standardized difference in composite scores (-0.06, 95% confidence interval -0.22 to 0.09) was not significant (2-tailed  $p = 0.33$ ). Differences were similar in early and late postmenopause groups (2-tailed interaction  $p = 0.88$ ). Interactions between postmenopause groups and differences between treatment groups were not significant for executive functions or global cognition. **CONCLUSIONS:** Estradiol initiated within 6 years of menopause does not affect verbal memory, executive functions, or global cognition differently than therapy begun 10+ years after menopause. Estradiol neither benefits nor harms these cognitive abilities regardless of time since menopause. **CLASSIFICATION OF EVIDENCE:** This study provides Class I evidence that estradiol initiated within 6 years of menopause does not affect cognition at 2.5 years differently than estradiol initiated 10+ years after menopause.

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### **Sedentary Lifestyle and High-Carbohydrate Intake are Associated with Low-Grade Chronic Inflammation in Post-Menopause: A Cross-sectional Study.**

Alves BC, Silva TR, Spritzer PM.

**Introduction** Cardiovascular disease (CVD) is the leading cause of death in post menopausal women, and inflammation is involved in the atherosclerosis process. **Purpose** to assess whether dietary pattern, metabolic profile, body composition and physical activity are associated with low-grade chronic inflammation according to high-sensitivity C-reactive protein (hs-CRP) levels in postmenopausal women. **Methods** ninety-five postmenopausal participants, with no evidence of clinical disease, underwent anthropometric, metabolic and hormonal assessments. Usual dietary intake was assessed with a validated food frequency questionnaire, habitual physical activity was measured with a digital pedometer, and body composition was estimated by bioelectrical impedance analysis. Patients with hs-CRP  $\geq 10$  mg/L or using hormone therapy in the last three months before the study were excluded from the analysis. Participants were stratified according to hs-CRP lower or  $\geq 3$  mg/L. Sedentary lifestyle was defined as walking fewer than 6 thousand steps a day. Two-tailed Student's t-test, Wilcoxon-Mann-Whitney U or Chi-square ( $\chi^2$ ) test were used to compare differences between groups. A logistic regression model was used to estimate the odds ratio of variables for high hs-CRP. **Results** participants with hs-CRP  $\geq 3$  mg/L had higher body mass index (BMI), body fat percentage, waist circumference (WC), triglycerides, glucose, and homeostasis model assessment of insulin resistance (HOMA-IR) ( $p = 0.01$  for all variables) than women with hs-CRP  $< 3$  mg/L. Also, women with hs-CRP  $\geq 3$  mg/L had a higher glycemic load diet and lower protein intake. Prevalence of sedentary lifestyle ( $p < 0.01$ ) and metabolic syndrome ( $p < 0.01$ ) was higher in women with hs-CRP  $\geq 3$  mg/L. After adjustment for age and time since menopause, the odds ratio for hs-CRP  $\geq 3$  mg/L was higher for sedentary lifestyle (4.7, 95% confidence interval [95%CI] 1.4-15.5) and carbohydrate intake (2.9, 95%CI 1.1-7.7). **Conclusions** sedentary lifestyle and high-carbohydrate intake were associated with low-grade chronic inflammation and cardiovascular risk in postmenopause.

**J Exerc Rehabil. 2016 Jun 30;12(3):238-46. doi: 10.12965/jer.1632584.292. eCollection 2016.**

### **Low estrogen levels and obesity are associated with shorter telomere lengths in pre- and postmenopausal women.**

Shin YA, Lee KY.

The aim of this study was to determine whether there is an association between leukocyte telomere length (LTL), and estrogen level, oxidative stress, cardiovascular disease (CVD) risk factors, and cardiorespiratory fitness (CRF) in pre- and postmenopausal obese women. Fifty-four obese women (premenopausal, n=25; postmenopausal, n=29) were selected to participate in this study. The outcome measurements in the pre- and postmenopausal groups were compared using independent t-tests and Pearson correlation analysis. The estrogen level (P<0.001), LTL (P<0.05), high-density lipoprotein level (P<0.05), and CRF (P<0.001) were higher in premenopausal women than in postmenopausal women. The body fat percentage (P<0.05) and triglyceride concentration (P<0.05) were lower in premenopausal women than in postmenopausal women. There were no significant associations between LTL, CVD risk, CRF, and oxidative stress and antioxidant enzyme activity in pre-menopausal women. The body mass index (BMI) and body fat percent-age in postmenopausal women were negatively associated with LTL (P<0.05). When all women were considered (i.e., both pre- and post-menopause), the BMI, percentage of fat, and waist circumference had a negative association with LTL (P<0.05), and estrogen levels were positively associated with LTL (P<0.05). Decreased estrogen levels after menopause, a pivotal factor in the biology of aging, and obesity were more associated with shorter telomere lengths in pre- and postmenopausal women than aerobic capacity and other CVD risk factors.

**Stem Cells Dev. 2016 Jul 14. [Epub ahead of print]  
miRNAs related to skeletal diseases.**

Seeliger C, Balmayor ER, van Griensven M.

miRNAs as non-coding, short, double-stranded RNA segments are important for cellular biological functions such as proliferation, differentiation and apoptosis. miRNAs mainly contribute to the inhibition of important protein translations via their cleavage or direct repression of target messenger RNAs expressions. In the last decade, miRNAs got in the focus of interest with new publications on miRNAs in the context of different diseases. For many types of cancer or myocardial damage, typical signatures of local or systemically circulating miRNAs have already been described. However, little is known about miRNA expressions and their molecular effect in skeleton diseases. An overview of published studies reporting miRNAs detection linked with skeletal diseases was conducted. All regulated miRNAs were summarized and their molecular interactions were illustrated. This review summarizes the involvement and interaction of miRNAs in different skeletal diseases. Thereby, 59 miRNAs were described to be deregulated in tissue, cells or in the circulation of osteoarthritis, 23 miRNAs deregulated in osteoporosis and 107 miRNAs deregulated in osteosarcoma. The molecular influences of miRNAs regarding osteoarthritis, osteoporosis and osteosarcoma were illustrated. Specific miRNA signatures for skeletal diseases are described in the literature. Some overlapped, but also unique ones for each disease exist. These miRNAs may present useful targets for the development of new therapeutic approaches and are candidates for diagnostic evaluations.

**Healthcare (Basel). 2016 Jul 13;4(3). pii: E42. doi: 10.3390/healthcare4030042.**

**Association of Mid-Life Changes in Body Size, Body Composition and Obesity Status with the Menopausal Transition.**

Karvonen-Gutierrez C, Kim C.

The mid-life period is a critical window for increases in body weight and changes in body composition. In this review, we summarize the clinical experience of the menopausal transition by obesity status, and examine the evidence regarding the menopausal transition and reproductive hormones effects on body weight, body composition, or fat distribution. Mid-life obesity is associated with a different menopausal experience including associations with menstrual cycle length prior to the final menstrual period (FMP), age at the FMP, and higher prevalence of vasomotor symptoms. The menopausal transition is associated with weight gain and increased central body fat distribution; the majority of evidence suggests that changes in weight are due to chronological aging whereas changes in body composition and fat distribution are primarily due to ovarian aging. Continuous and regular physical activity during mid-life may be an efficacious strategy to counteract the age-related and menopause-related changes in resting energy expenditure and to prevent weight gain and abdominal adiposity deposition.

**Cancer Res. 2016 Jul 14. [Epub ahead of print]**

**Dietary Weight Loss and Exercise Effects on Serum Biomarkers of Angiogenesis in Overweight Postmenopausal Women: A Randomized Controlled Trial.**

Duggan C, Tapsoba JD, Wang CY, McTiernan A.

Obese and sedentary persons have an increased risk for cancer, but underlying mechanisms are poorly understood. Angiogenesis is common to adipose tissue formation and remodeling, and to tumor vascularization. A total of 439 overweight/obese, healthy, postmenopausal women [body mass index (BMI) > 25 kg/m<sup>2</sup>] ages 50-75 years, recruited between 2005 and 2008 were randomized to a 4-arm 12-month randomized controlled trial, comparing a caloric restriction diet arm (goal: 10% weight loss, N = 118), aerobic exercise arm (225 minutes/week of moderate-to-vigorous activity, N = 117), a combined diet + exercise arm (N = 117), or control (N = 87) on circulating levels of angiogenic biomarkers. VEGF, plasminogen activator inhibitor-1 (PAI-1), and pigment epithelium-derived factor (PEDF) were measured by immunoassay at baseline and 12 months. Changes were compared using generalized estimating equations, adjusting for baseline BMI, age, and race/ethnicity. Participants randomized to the diet + exercise arms had statistically significantly greater reductions in PAI-1 at 12 months compared with controls (-19.3% vs. +3.48%, respectively, P < 0.0001). Participants randomized to the diet and diet + exercise arms had statistically significantly greater reductions in PEDF (-9.20%, -9.90%, respectively, both P < 0.0001) and VEGF (-8.25%, P = 0.0005; -9.98%, P < 0.0001, respectively) compared with controls. There were no differences in any of the analytes in participants randomized to the exercise arm compared with controls. Increasing weight loss was statistically significantly associated with linear trends of greater reductions in PAI-1, PEDF, and VEGF. Weight loss is significantly associated with reduced circulating VEGF, PEDF, and PAI-1, and could provide incentive for reducing weight as a cancer prevention method in overweight and obese individuals

**Osteoporos Int. 2016 Jul 14. [Epub ahead of print]**

### **Measurements of skeletal muscle mass and power are positively related to a Mediterranean dietary pattern in women.**

Kelaiditi E, Jennings A, Steves CJ, Skinner J, Cassidy A, MacGregor AJ, Welch AA.

**INTRODUCTION:** The loss of skeletal muscle mass, strength, and function with age are contributing risk factors for the onset of sarcopenia, frailty, osteoporosis, fractures, and mortality. Nutrition may affect the progression and trajectory of these changes in skeletal muscle but the role of the micronutrient-rich Mediterranean diet (MD) has hardly been investigated in relation to these muscle outcomes. **METHODS:** We examined associations between the MD score (MDS) and FFM% (fat-free mass / weight × 100), FFMI (fat-free mass/height<sup>2</sup>), hand grip strength, and leg explosive power (LEP, watts/kg) in a cross-sectional study in 2570 women aged 18-79 years from the TwinsUK study. Measurements of body composition were made using dual-energy X-ray absorptiometry and dietary intake assessed by a food frequency questionnaire. FFM%, FFMI, grip strength, and LEP were compared across quartiles of the MDS after adjustment for covariates, with CRP measured in a subgroup (n = 1658). **RESULTS:** Higher adherence to the MDS was positively associated with measurements of muscle outcomes, with significant differences of 1.7 % for FFM% and 9.6 % for LEP (P trend < 0.001), comparing extreme quartiles of intake, but not with grip strength or CRP concentrations. **CONCLUSIONS:** For the first time in a northern European population, we have observed significant positive associations between the MDS and FFM% and LEP in healthy women that are potentially clinically relevant, independent of the factors known to influence muscle outcomes. Our findings emphasize the potential role for overall diet quality based on the MD in the prevention of age-related loss of skeletal muscle outcomes.

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### **Hot Flash Frequency and Blood Pressure: Data from the Study of Women's Health Across the Nation.**

Jackson EA, El Khoudary SR, Crawford SL, Matthews K, Joffe H, Chae C, Thurston RC.

**BACKGROUND:** Vasomotor symptoms (VMS) are highly prevalent among midlife women and have been associated with subclinical cardiovascular disease (CVD). However, the association between VMS frequency and risk factors such as hypertension (HTN) remains unclear. **MATERIALS AND METHODS:** We examined VMS frequency and blood pressure (BP) among 2839 participants of the Study of Women's Health Across the Nation (SWAN), a multiethnic, prospective, study of women enrolled from seven U.S. sites between November 1995 and October 1997. Women were age 42-52, with no history of CVD, and not postmenopausal at baseline. VMS was defined by the number of days a woman reported VMS over the 2-week period before each annual visit. Frequent VMS was defined as ≥6 days of VMS; less frequent VMS was defined 1-5 days of symptoms with asymptomatic women the reference group. BP was measured at each visit in addition to demographic and clinic factors. **RESULTS:** At baseline, 298 women reported frequent VMS, 794 less frequent VMS and 1747 no VMS. More frequent baseline VMS was associated with higher BP. Compared to no VMS, baseline VMS was associated with HTN (odds ratio [OR] 1.47, 95% confidence interval [CI]; 1.14-1.88 for infrequent VMS, and OR 1.40, (95% CI; 0.97-2.02 for frequent VMS). Risk for incident pre-HTN or HTN during follow-up was increased among women with frequent VMS (hazard ratio of 1.39, 95% CI; 1.09-1.79) after adjustment for multiple covariates.

**CONCLUSION:** Women with VMS may be more likely to develop HTN compared to women without VMS. Further research related to VMS including frequency of symptoms is warranted.